N-Aminoazoles. Part 2.[1] Basicity and Protonation Site of *N*-Aminoazoles: an Experimental (pK_a, ^{13}C and ^{15}N NMR Spectroscopy and Crystallography) and Theoretical Study

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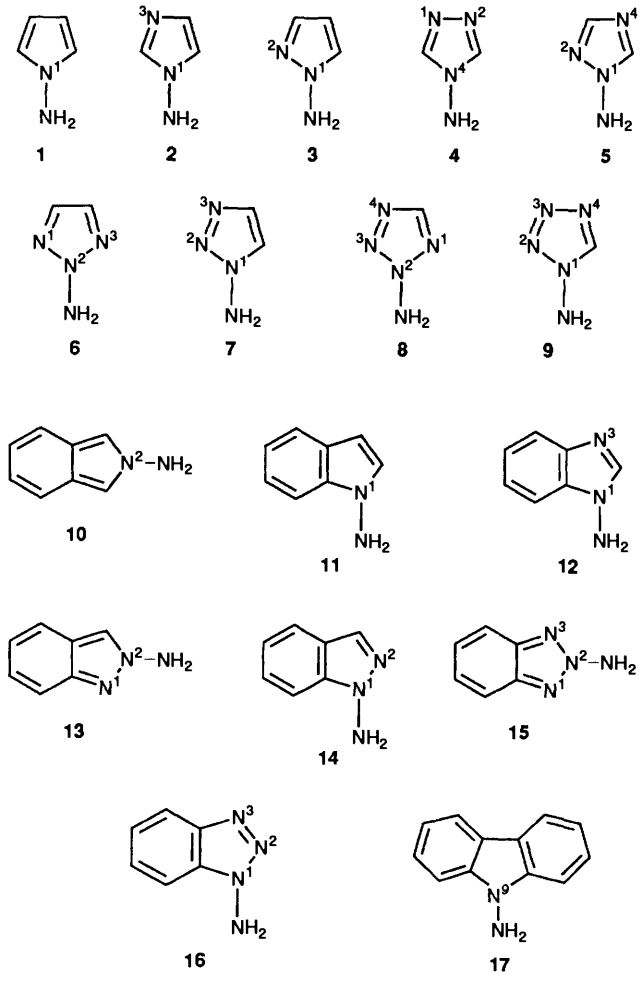
The ^{13}C and ^{15}N NMR spectra of 1-aminoimidazole **2**, 1-aminopyrazole **3**, 4-amino-1,2,4-triazole **4**, 1-amino-1,2,4-triazole **5**, 1-aminobenzimidazole **12**, 2-aminoindazole **13**, 1-aminoindazole **14**, 2-aminobenzotriazole **15** and 1-aminobenzotriazole **16** have been recorded in neutral ($CDCl_3$ or [$^2H_6$]DMSO) and acid (CF_3CO_2H and SO_4H_2) conditions. The X-ray crystal structures of two polymorphic forms of *N*-aminobenzimidazolium picrate **12d** have been determined. The main differences between the forms are due to the twist of an *ortho*-nitro group of the picrate anion up to 53° leading to a different hydrogen bond network. In the two crystals, the relative disposition of both ions is similar being held together by $N^+–H\cdots O^-/O_2N$ three centre hydrogen bonds. The basic pK_as of 1-aminoindole **11**, compounds **12** and **13** and 9-aminocarbazole **17** have been measured. Finally, all monoprotonated cations on *N*-aminoazoles (from pyrrole **1** to carbazole **17**) have been calculated. When there is a pyridine-like nitrogen atom on the ring, this is the preferred site of protonation although in sulfuric acid the amino group is also protonated, only 1-aminoindole and 9-aminocarbazole protonate on the amino group.

N-Aminoazoles are a family of compounds of increasing interest. Some time ago,[1] we described the structure of these compounds using X-ray crystallography (the structures of 1-aminobenzimidazole **12** and 2-aminobenzotriazole **15** were reported), ^{15}N NMR spectroscopy (ten compounds) and INDO calculations on all the parent compounds (17 derivatives from 1-aminopyrrole **1** to 9-aminocarbazole **17**). The most important conclusions of that study concerned the hybridisation and conformation of the amino group: (i) sp^3 hybridisation is always favoured over sp^2; (ii) for monocyclic azoles **1**–**9** the parallel conformations (∥, *i.e.*, those in which the amino lone pair eclipses the ring, $\alpha = 90°$ or 90°') which avoid lone pair–lone pair repulsions are always the most stable; and (iii) the perpendicular conformations (⊥, *i.e.*, those in which the amino lone pair is perpendicular to the ring plane, $\alpha = 0°$) appear to be the most stable only for 2-substituted benzazoles **10**, **13** and **15**. In addition to this work, results from other authors deserve to be reported. The crystal structure of 3-methyl-4-amino-5-thioxo-1,2,4-triazole **18** shows that the amino group is in a parallel conformation with the lone pair antiperiplanar to the thione ($\alpha = 90°$).[2] The structures of 1-amino-3-phenylpyrazole **19**, 1-amino-5-methyl-3-phenylpyrazole **20** and 1-amino-5-methyl-4-methoxycarbonylpyrazole **21** correspond to planar conformations with antiperiplanar lone pairs (α between 81 and 83°).[3] A series of papers by Pozharskii concerning the crystal structures of 1-methyl-9-aminoxanthine **22**[4] and that of a derivative of 1-amino-3-methylbenzimidazoline **23**[5] and the pK_as of a series of 1-aminobenzimidazoles[6] are worth noting.

In structure **22** the amino group is in a parallel conformation with the lone pair directed towards C(2) ($\alpha = 90°$); in compound **23**, due to an intramolecular hydrogen bond, an N–H pointed towards the carbonyl group.



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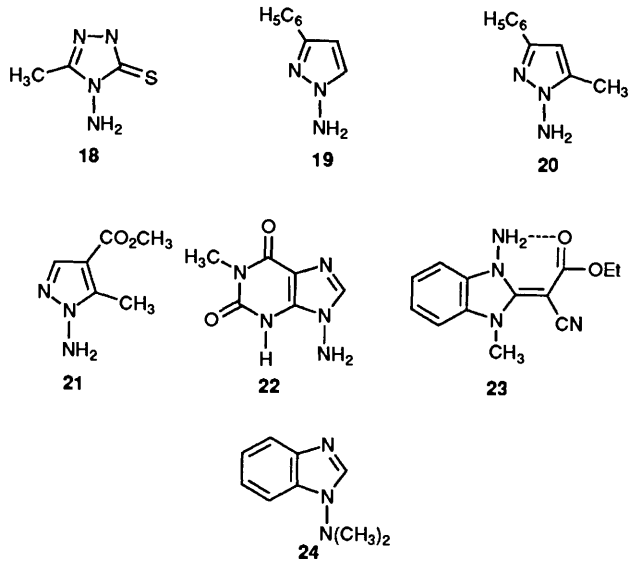
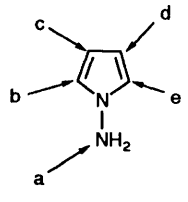


Table 1 All possible monoprotonated salts corresponding to *N*-aminoazoles

	On the amino group	On the ring nitrogens
1-Aminopyrrole **1**	**1a**	—
1-Aminoimidazole **2**	**2a**	N^3 **2c**
1-Aminopyrazole **3**	**3a**	N^2 **3b**
4-Amino-1,2,4-triazole **4**	**4a**	N^1 (≡N^2) **4c 4d**
1-Amino-1,2,4-triazole **5**	**5a**	N^2 **5b** or N^4 **5d**
2-Amino-1,2,3-triazole **6**	**6a**	N^1 (≡N^3) **6b 6e**
1-Amino-1,2,3-triazole **7**	**7a**	N^2 **7b** or N^3 **7c**
2-Aminotetrazole **8**	**8a**	N^3 **8b**, on N^4 **8c** or N^1 **8e**
1-Aminotetrazole **9**	**9a**	N^2 **9b**, on N^3 **9c** or N^4 **9d**
1-Aminoindole **11**	**11a**	—
1-Aminobenzimidazole **12**	**12a**	N^3 **12d**
2-Aminoindazole **13**	**13a**	N^1 **13b**
1-Aminoindazole **14**	**14a**	N^2 **14e**
2-Aminobenzotriazole **15**	**15a**	N^1 (≡N^3) **15b 15e**
1-Aminobenzotriazole **16**	**16a**	N^2 **16e** or N^3 **16d**
9-Aminocarbazole **17**	**17a**	—

Recently the structure of *N*-aminopentazole has been calculated with a basis set of DZP quality.[7] The geometry corresponding to the most stable structure follows rules (i) (sp^3 nitrogen) and (ii) (parallel conformation).

All this information about neutral *N*-aminoazoles contrasts with the paucity of data concerning their salts: only the pK_as of some *N*-aminoazoles in acetonitrile at 20 °C have been described (**11**, pK_a = 6.55; **12**, pK_a = 12.83; **13**, pK_a = 8.64; **14**, pK_a = 6.70; 1-dimethylaminobenzimidazole **24**, pK_a = 12.40).[6] It was thus decided to study the protonation site of *N*-aminoazoles using X-ray crystallography, ^{13}C and ^{15}N NMR spectroscopy and to determine the basicity of some of them. To discuss the experimental data, INDO//INDO calculations were performed on all the possible protonated forms. Previously, a ^{13}C and ^{15}N NMR study of the corresponding *N*-methyl derivatives was carried out.[8]



To describe the structure of the cations obtained by protonation of *N*-aminoazoles, the above scheme has been adopted. The number of the compound followed by the letter **a** means that the salt is protonated on the amino group; the other letters stand for nitrogen atoms occupying ring positions. This has been necessary since the numbering in *N*-aminoazoles changes with the heterocycle. To avoid confusion, all the possible *N*-monoprotonated cations have been collected in Table 1.

Experimental

All the compounds have been described.[1] Ionisation constants (thermodynamic pK_as) were determined spectrophotometrically.[9] The different pH values, from 0 to 10, were obtained by addition of either NaOH (5 mol dm^{-3}) or H_2SO_4 (3.5 mol dm^{-3}) to the aqueous solutions of the *N*-aminobenzazoles, checking that the same total concentration of the chromophore was present in all cases after the pH adjustment. The 'analytical wavelength'[9] was 288, 274, 280 and 285 nm for compounds **11**, **12**, **13** and **17**. Due to the low solubility of these compounds in water, typical optical densities were in the order of 0.1 at those wavelengths. Reversibility of the protonation–deprotonation process was checked in all cases. The absorption spectra were measured with a Shimadzu UV-2100 spectrophotometer and a matched pair of Suprasil cells of 1 cm thickness at 25.0 ± 0.1 °C (Heto thermostat). The solutions were prepared employing doubly deionised water (Milli-Q) and freshly open ampoules of H_2SO_4 and NaOH Fixanal from Riedel-de-Haen. The pK_as are reported in Table 2.

NMR spectra were obtained on a Bruker AC-200 instrument operating at 200.13, 50.32 and 20.29 MHz with standard conditions. Chemical shifts (δ) and coupling constants (J/Hz) were measured in the solvent specified in each case referred to Me_4Si as internal standard for ^1H and ^{13}C NMR and to external nitromethane for ^{15}N NMR. An inner [$^2H_6$]DMSO capillary tube was used to provide the lock for all experiments where H_2SO_4 and CF_3CO_2H were used as solvents.

Crystal Structure Determination.—Yellow crystals suitable for the X-ray analysis were obtained by slow evaporation of an ethanolic solution of 1-aminobenzimidazolium picrate **12d**. Since two types of crystal habits could be detected, prisms **I** and plates **II**, it was decided to collect the corresponding spectra. Crystal data and the main experimental details are given in Table 3. The two picrates have the same melting point, 223–226 °C, but both show under the microscope a transition at 145 °C.

Both structures were solved by direct methods[14] and they reveal that we are dealing with two polymorphic crystals. The non-hydrogen atoms were refined anisotropically and then the hydrogens were included and refined as isotropic. Most of the calculations were performed using the XRAY80 System[15] on a VAX6410 computer. The atomic scattering factors were taken from ref. 16.

Results and Discussion

Crystal and Molecular Structure of 1-*Aminobenzimidazolium Picrates* **12d**.—The structure of guanazine (3,4,5-triamino-1,2,4-triazole) hydrobromide[13] is the only example of crystal structure of an *N*-aminoazole salt. Although it protonates on N^1, the positive charge is delocalised between the 1,2,4-triazole ring and one of the *C*-amino groups, thus guanazine hydrobromide is not a clean example of protonation on the azole. Its amino group shows a parallel conformation with α = 90°.

Both picrates, **12dI** and **12dII**, have as common features the molecular structure of the *N*-aminobenzimidazolium moiety and its relative disposition with respect to the picrate anion, Fig. 1 and Table 4.

Table 2 Thermodynamic pK_as of *N*-aminoazoles and the corresponding *N*-methylazoles

	Compound	pK_a	Compound	pK_a
4	4-Amino-1,2,4-triazole	2.25[10]	4-Methyl-1,2,4-triazole	3.40[11]
11	1-Aminoindole	1.43 ± 0.04[a]	1-Methylindole	−2.56[12]
12	1-Aminobenzimidazole	4.95 ± 0.07[a]	1-Methylbenzimidazole	5.55[11]
13	2-Aminoindazole	1.44 ± 0.18[a]	2-Methylindazole	2.01[11]
17	9-Aminocarbazole	1.50 ± 0.10[a]	9-Methylcarbazole	−5.89[12]

[a] This work.

Table 3 Crystal analysis parameters at room temperature

	I	**II**
Crystal data		
Formula	$C_7H_8N_3{}^+C_6H_2N_3O_7{}^-$	$C_7H_8N_3{}^+C_6H_2N_3O_7{}^-$
Crystal habit	Yellow prism	Yellow plate
Crystal size/mm	0.10 × 0.13 × 0.46	0.07 × 0.30 × 0.33
Symmetry	Orthorhombic, *Pbca*	Triclinic, *P*-1
Unit cell determination	Least-squares fit from 67 reflections (θ < 45°)	Least-squares fit from 74 reflections (θ < 45°)
Unit cell dimensions (Å, °)	*a* = 24.7912(12)	*a* = 8.3658(3)
	b = 16.8372(7)	*b* = 12.7514(9)
	c = 7.1112(1)	*c* = 7.6572(3)
	90, 90, 90	102.320(5), 103.277(3), 73.348(5)
Packing: V/Å^3, Z	2968.3(2), 8	752.1(1), 2
D_c/g cm^{-3}, M, F(000)	1.621, 362.26, 1488	1.600, 362.26, 372
μ/cm^{-1}	11.18	11.03
Experimental data		
Technique	Four circle diffractometer: Philips PW1100, bisecting geometry Graphite oriented monochromator: CuKα, $\omega/2\theta$ scans, scan width 1.4° Detector apertures 1 × 1°. θ_{max} = 65°, 1 min/reflex.	
Number of reflections: Independent	2534	2561
Observed	1949 [3$\sigma(I)$ criterion]	2293 [3$\sigma(I)$ criterion]
Standard reflections:	2 reflections every 90 min. No variation	
Solution and refinement		
Solution	Direct methods: SIR88	
Refinement: Least-squares on F_o	Full matrix	
Parameters:		
Number of variables	275	275
Degrees of freedom	1674	2018
Ratio of freedom	7.1	8.3
Final shift/error	0.09	0.09
H atoms	From difference synthesis	
Weighting-scheme	Empirical as to give no trends in $\langle\omega\Delta^2F\rangle$ *vs.* $\langle\|F_{obs}\|\rangle$ and $\langle\sin\theta/\lambda\rangle$	
Max. thermal value/Å^2	*U*33[O(25)] = 0.322(8)	*U*22[O(19)] = 0.171(3)
Final ΔF peaks/e Å^{-3}	0.42 near O(20)	0.34 near N(18)
Final R and R_w	0.056, 0.060	0.050, 0.058

The *N*-aminobenzimidazolium cations are not different, in terms of the achieved precision,[17] and present a significant lack of planarity, χ^2 = 176.38 and 180.00 *vs.* the tabulated value of 12.60 (95%).[18] The amino group displays sp^3 hybridization and a staggered conformation with respect to C(71), in a similar way to that shown by the unprotonated molecule, **12**.[1] Bond distances and angles in the five-membered rings reflect the effect of protonation giving rise to an almost symmetrical ring with respect to a line through C(2) and the midpoint of the C(31)–C(71) bond. The discrepancies between both polymorphic forms arise from the different conformations of one of the three nitro groups [C(11)–C(12)–N(18)–O(19) = −52.8° in **II**] which lead to different *endo*- and *exo*-cyclic angular deformations in the picrate anion, the main ones being C(11)–C(12)–C(13) > C(11)–C(16)–C(15), C(14)–C(15)–C(16) > C(12)–C(13)–C(14) and C(16)–C(11)–O(17) > C(12)–C(11)–O(17). The picrate phenyl ring only deviates significantly from planarity in the polymorphic form **I** [χ^2 = 59.01 and 6.62 *vs.* 7.81 (95%) for **I** and **II** respectively].

The deformations caused by the substituents on the phenyl ring of the picrate anion are more evident in the C(11)–C(12) and C(11)–C(16) distances and in all *endo*-cyclic angles. That at C(11) differs considerably from 120°, Table 4. In order to study the influence of the substituents O^- and NO_2 on benzene geometries, a retrieval of picrate anions from the Cambridge Structural Database (CSD)[19] was carried out. Only 25 fragments fulfilling the following conditions were retained: no metals, no disorder, hydrogen atoms present and an R < 0.075. The nitro groups at *para* position are twisted less than 18° while those at *ortho* positions are twisted up to 66°. The data were separated in two groups, one with C–C–N–O torsion angle, τ, less than 30° and the other from 30° upwards. The averaged geometries of the picrate anions are in agreement with those of polymorphs **I** and **II**, Table 4.

A theoretical calculation at the AM1 level,[20] of the picrate moiety indicates that all distances in the benzene ring are larger than the corresponding experimental ones, the pattern of endocyclic angles is less distorted and the C–O and N–O distances shorter than the observed in the solid state, possibly due to the presence of hydrogen bond interaction in the crystals. The minimum energy conformation has the nitro groups at positions 2, 4 and 6 twisted by 19.0°, −0.4° and −17.0° with respect

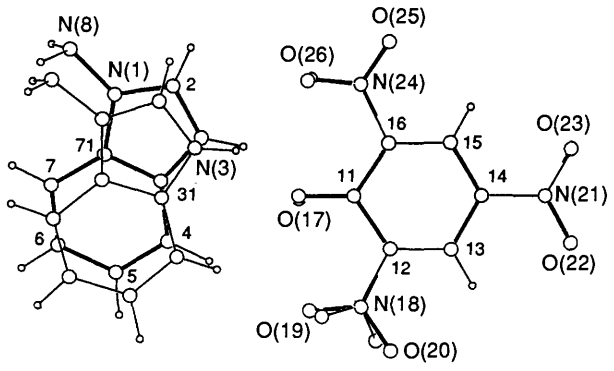


Fig. 1 Perspective view of the crystallographic asymmetric unit of both polymorphs superimposed as projection on the picrate ring showing the atom labelling scheme. The thin line corresponds to form **II**.

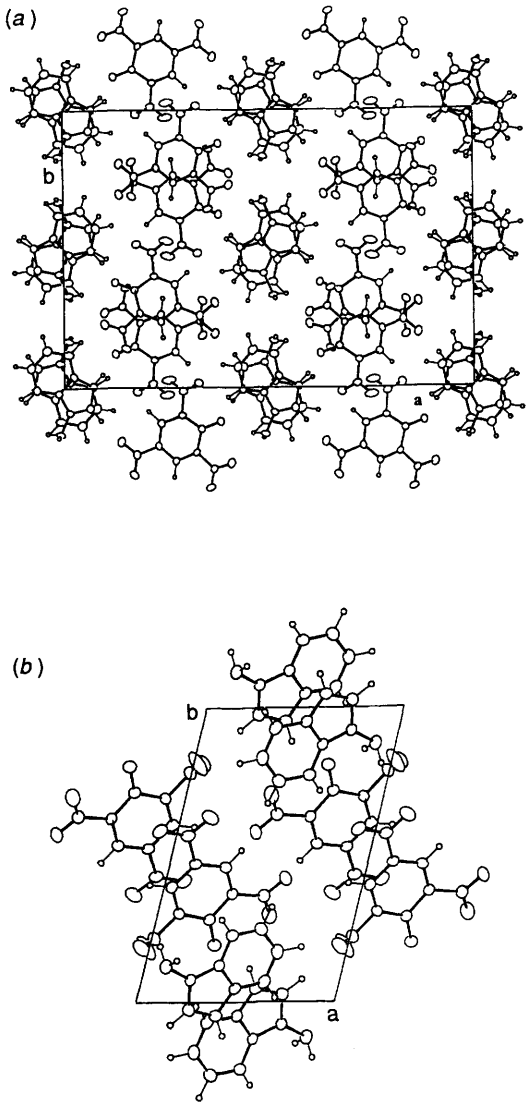


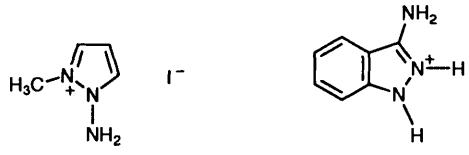
Fig. 2 Packing diagrams of the polymorphic forms **I** and **II** projected along the *c*-axis

to the benzene plane, Table 4. About 0.01 and 0.82 kcal mol^{-1} are required to bring the τ angles to those of experimental values for **I** and **II** respectively.

Both ions, *N*-aminobenzimidazolium and picrate, are held together by a three centre hydrogen bond, N^+–H · · · $^-$O–Ar and N^+–H · · · O_2N–Ar, the last one being weaker in **II** than in **I**, 3.093(3) *vs.* 2.800(4) Å, respectively. Moreover, a different hydrogen bonding pattern is exhibited in both crystals. Details of the hydrogen networks are given in Table 5. The packing of polymorph **I** presents piles of cations and piles of anions parallel to each other along the *c*-axis in such a way that the crystal can be built of layers of anions and cations along the *a*-axis, Fig. 2. The cations present alternating averaged distances between their planes of 3.364(1) and 3.238(1) Å, suggesting π interactions between them, however the offset of the anions does not allow this type of interaction. The main peculiarity of the crystal packing of form **II** is the overlapping of the cations through a symmetry centre, the distance between their planes being 3.299(1) Å, Fig. 2.

^{13}C and ^{15}N Chemical Shifts and Coupling Constants of Protonated N-Aminoazoles.—In a preceding paper, dealing with *N*-methylazoles,[8] we described the effects of the protonation on the ^{13}C and ^{15}N NMR chemical shifts and ^{1}H–^{13}C coupling constants as well as the preferred protonation site. This site, deduced from these protonation induced shifts (PIS), was consistent with *ab initio* calculations of all possible cations. There are few other relevant studies, the two most significant reported the use of ^{15}N NMR spectroscopy for the determination of the protonation site of *C*-aminopyrazoles[21] and *C*-amino-1,2,4-triazoles.[22]

The ^{13}C NMR results are reported in Tables 6 and 7. The chemical shifts of neutral compounds **12** and **13** are consistent with those previously described.[23] Compound **25**, 1-amino-2-methylpyrazolium iodide,[24] has been added to Table 6 as a model of protonation at position 2 of the 1-aminopyrazole **3b**. Clearly **3b** and **25** have very close chemical shifts and coupling constants, thus proving their electronic similarity. An increase of the ^{1}H–^{13}C coupling constants upon protonation is observed but, as we have pointed out before,[8] this increase is unspecific and cannot be used to assign the protonation site, only to assert that the protonation takes place on the azole ring.



25 **26**

The ^{15}N NMR chemical shifts and some ^{1}H–^{15}N coupling constants are gathered in Table 8 [$^1J(^1H–^{15}N)$ coupling constants are given in absolute values]. The values for the neutral compounds are those of ref. 1. A first important observation is that although the chemical shifts determined in CF_3CO_2H and H_2SO_4 are different, they are linearly related.

$$NH_2: \delta_{^{15}N}(SO_4H_2) = -52.7 + 0.82\,\delta_{^{15}N}(TFA); \quad n = 8, R = 0.99 \quad (1)$$

$$N\text{–}NH_2: \delta_{^{15}N}(SO_4H_2) = -18.4 + 1.01\,\delta_{^{15}N}(TFA); \quad n = 8, R = 0.99 \quad (2)$$

$$N(sp^2): \delta_{^{15}N}(SO_4H_2) = -14.6 + 0.92\,\delta_{^{15}N}(TFA); \quad n = 10, R = 0.99 \quad (3)$$

These equations show that the structure of the cations formed in both acids are the same, the differences being unspecific are attributable to solvent effects (including hydrogen bonds) and not to a double protonation in sulfuric acid. For *C*-aminoazoles where double protonation (in the ring and on the amino group) is observed in sulfuric acid,[21] larger and opposite sign effects are observed.

We have previously described that 1-aminopyrazole **3** and 1-

Table 4 Selected bond distances and angles and torsion angles (Å, °)

(a) Benzimidazolium	I	II	Benzimidazole[1]		
N(1)–C(2)	1.329(4)	1.328(3)	1.363(3)		
N(1)–C(71)	1.386(4)	1.388(3)	1.367(3)		
N(1)–N(8)	1.412(4)	1.404(3)	1.408(3)		
C(2)–N(3)	1.325(4)	1.318(3)	1.308(3)		
N(3)–C(31)	1.391(4)	1.391(3)	1.390(3)		
C(31)–C(4)	1.392(5)	1.388(4)	1.396(4)		
C(31)–C(71)	1.383(4)	1.387(3)	1.398(3)		
C(71)–N(1)–N(8)	127.4(3)	128.0(2)	129.0(2)		
C(2)–N(1)–N(8)	123.5(3)	123.2(2)	123.3(2)		
C(2)–N(1)–C(71)	109.1(3)	108.8(2)	107.6(2)		
N(1)–C(2)–N(3)	109.4(3)	109.9(2)	112.7(2)		
C(2)–N(3)–C(31)	108.9(3)	108.8(2)	104.9(2)		
N(3)–C(31)–C(71)	106.4(3)	106.4(2)	109.9(2)		
N(1)–C(71)–C(31)	106.3(3)	106.1(2)	104.9(2)		
C(71)–N(1)–N(8)–H(81)	54(3)	−61(3)	−59(2)		
C(71)–N(1)–N(8)–H(82)	−64(3)	62(3)	58(2)		
(b) Picrate	I	II	CSD(|τ| < 30°)	CSD(|τ| > 30°)	AM1
C(11)–C(12)	1.448(4)	1.444(3)	1.456(4)	1.449(10)	1.472
C(12)–C(13)	1.372(4)	1.363(3)	1.371(3)	1.367(4)	1.380
C(13)–C(14)	1.381(4)	1.391(3)	1.382(4)	1.388(6)	1.412
C(14)–C(15)	1.386(4)	1.378(4)	1.382(4)	1.385(7)	1.412
C(15)–C(16)	1.372(4)	1.374(3)	1.371(3)	1.374(7)	1.380
C(11)–C(16)	1.450(4)	1.444(3)	1.456(4)	1.451(9)	1.472
C(11)–O(17)	1.251(4)	1.250(2)	1.243(4)	1.249(10)	1.239
C(12)–N(18)	1.455(4)	1.459(3)	1.455(7)	1.457(7)	1.472
C(14)–N(21)	1.440(4)	1.438(3)	1.448(9)	1.446(8)	1.459
C(16)–N(24)	1.460(4)	1.450(3)	1.455(7)	1.448(8)	1.472
N(18)–O(19)	1.203(4)	1.199(3)	1.215(22)	1.225(9)	1.201
N(18)–O(20)	1.204(4)	1.221(4)	1.217(19)	1.223(8)	1.212
N(21)–O(22)	1.213(4)	1.220(3)	1.227(5)	1.228(8)	1.208
N(21)–O(23)	1.218(4)	1.219(3)	1.227(5)	1.228(8)	1.208
N(24)–O(25)	1.197(6)	1.222(3)	1.215(22)	1.224(12)	1.212
N(24)–O(26)	1.207(4)	1.219(3)	1.217(19)	1.223(10)	1.201
C(12)–C(11)–C(16)	111.8(3)	111.8(2)	111.4(4)	111.6(8)	113.2
C(11)–C(12)–C(13)	124.6(3)	125.8(2)	124.3(5)	125.2(6)	123.0
C(12)–C(13)–C(14)	118.9(3)	117.7(2)	119.2(5)	118.4(5)	120.1
C(13)–C(14)–C(15)	121.4(3)	121.2(2)	121.4(5)	121.2(4)	120.2
C(14)–C(15)–C(16)	119.2(3)	120.1(2)	119.2(5)	119.7(6)	120.1
C(11)–C(16)–C(15)	124.1(3)	123.2(2)	124.3(5)	123.7(6)	123.0
C(16)–C(11)–O(17)	123.9(3)	126.5(2)	124.3(7)	125.6(8)	123.4
C(12)–C(11)–O(17)	124.3(3)	121.6(2)	124.3(7)	122.7(10)	123.4
C(11)–C(12)–N(18)	119.4(3)	117.1(2)	119.6(6)	118.2(13)	118.6
C(13)–C(12)–N(18)	116.0(3)	117.0(2)	116.0(5)	116.6(9)	118.5
C(13)–C(14)–N(21)	119.5(3)	118.5(2)	119.3(5)	119.4(5)	119.9
C(15)–C(14)–N(21)	119.2(3)	120.3(2)	119.3(5)	119.4(5)	119.9
C(15)–C(16)–N(24)	115.8(3)	116.8(2)	116.0(5)	116.2(5)	118.5
C(11)–C(16)–N(24)	120.1(3)	119.9(2)	119.6(6)	120.0(6)	118.6
C(11)–C(12)–N(18)–O(19)	12.9(4)	−52.8(3)	(−29.1–29.3)	(31.1–66.0)	19.0
C(13)–C(14)–N(21)–O(22)	0.2(5)	−10.0(3)	(−11.7–8.9)	(−17.3–16.5)	−0.4
C(15)–C(16)–N(24)–O(25)	−17.3(6)	15.4(3)	(−29.1–29.3)	(−27.3–15.9)	−17.0

aminoindazole **14** rearrange by heating in organic and inorganic acids to the corresponding 3-amino derivatives.[25,26] In the case of pyrazole, the ^{13}C and ^{15}N NMR spectra in CF_3CO_2H and H_2SO_4 correspond to protonated 1-aminopyrazole. According to Gasco,[21] the ^{15}N NMR spectra of 3- and 5-aminopyrazoles in CF_3CO_2H are characterised by a signal at −353 ppm corresponding to the amino group while for **3b**, the amino group appears at −305 ppm, as in other compounds of Table 8. On the other hand, the ^{13}C and ^{15}N NMR spectra of compound **14** in CF_3CO_2H are those of protonated 3-aminoindazole **26** ($\delta_{N^1} = -253.2$, $\delta_{N^2} = -228.3$, $\delta_{NH_2} = 324.6$). The product recovered from the NMR experiments shows a ^1H NMR spectrum which lacks the 3-H signal. Indole and carbazole derivatives, **11** and **17**, decompose in acid solution.

The clearest proof that protonation of *N*-aminoazoles takes place on the azole ring comes from the observation of $^1J(^1H–^{15}N)$ couplings in several cases (Table 8). These couplings are similar to those described for protonated pyridines and quinolines ($^1J \sim -95$ Hz)[27–29] and for protonated 1-methylimidazole ($^1J = -101.0$ Hz).[30] Even the long-range $^1H–^{15}N$ coupling constants of protonated 1-amino (Table 8) and 1-methyl-imidazole[30] are very similar.

The ^{13}C and ^{15}N protonation induced shifts (PIS) reported in Table 9 show that *N*-aminoazoles and *N*-methylazoles yield, on protonation, the same type of cations: both protonate in the ring and, if there are several basic nitrogen atoms, in the same position of the ring. For *N*-aminoazoles, the cations have the following structures: **2c**, **3b**, **4c** or **4d**, **5d**, **12d**, **13b**, **14e**, **15b** or

Table 5 Intermolecular interactions. Numbers stand for symmetry operations and C(1–71), C(31–71) and C(11–16) for the centroids of the corresponding rings (Å, °)

	Interatomic distances			
X–H···Y	X–H	X···Y	H···Y	X–H ···Y
(a) Compound **I**				
N(3)–H(3)···O(17)	0.97(5)	2.688(4)	1.82(5)	148(5)
N(3)–H(3)···O(26)	0.97(5)	2.800(4)	2.14(5)	124(4)
C(4)–H(4)···O(17)	1.04(4)	3.434(4)	2.84(4)	116(3)
C(4)–H(4)···O(19)	1.04(4)	3.686(5)	2.68(4)	163(3)
C(2)–H(2)···O(23)[1]	1.00(4)	3.042(4)	2.49(4)	115(3)
C(6)–H(6)···O(23)[2]	0.99(4)	3.311(4)	2.62(4)	127(3)
C(7)–H(7)···O(20)[3]	0.97(4)	3.486(5)	2.57(4)	157(3)
N(8)–H(82)···O(19)[3]	0.96(5)	2.980(5)	2.32(5)	126(4)
N(8)–H(81)···O(17)[4]	0.93(5)	3.199(4)	2.31(5)	161(4)
C(13)–H(13)···O(25)[5]	0.96(4)	3.587(4)	2.63(4)	176(3)
C(1–71)···C(31–71)[6]		3.627(2)		
C(1–71)···C(1–71)[4]		3.321(2)		
C(1–71)···C(31–71)[4]		3.554(2)		
C(31–71)···C(31–71)[6]		3.719(2)		

[1] $\frac{1}{2}-x,-y,\frac{1}{2}+z$. [2] $-\frac{1}{2}+x,y,\frac{3}{2}-z$. [3] $-x,-\frac{1}{2}+y,\frac{3}{2}-z$. [4] $-x,-y,1-z$. [5] $\frac{1}{2}-x,\frac{1}{2}+y,z$. [6] $-x,-y,2-z$.

(b) Compound **II**				
N(3)–H(3)···O(17)	0.93(3)	2.668(2)	1.85(4)	146(3)
N(3)–H(3)···O(26)	0.93(3)	3.093(3)	2.37(4)	133(3)
C(4)–H(4)···O(17)	0.95(3)	3.215(3)	2.64(3)	119(2)
C(2)–H(2)···O(19)[1]	0.94(4)	3.233(5)	2.32(3)	165(2)
C(5)–H(5)···O(20)[2]	1.01(4)	3.512(4)	2.61(4)	149(2)
C(6)–H(6)···O(23)[3]	0.95(3)	3.231(4)	2.54(3)	130(2)
N(8)–H(81)···O(23)[4]	0.91(4)	3.267(3)	2.59(3)	132(3)
C(7)–H(7)···O(22)[4]	0.99(3)	3.278(3)	2.35(3)	157(3)
N(8)–H(81)···O(20)[5]	0.91(4)	3.111(4)	2.52(4)	124(3)
N(8)–H(82)···O(19)[6]	0.92(4)	2.920(4)	2.32(4)	122(3)
N(8)–H(82)···O(17)[6]	0.92(4)	3.327(3)	2.44(4)	162(3)
C(13)–H(13)···O(25)[7]	0.97(3)	3.514(3)	2.61(3)	155(2)
C(1–71)···C(1–71)[6]		3.385(1)		
C(1–71)···C(31–71)[6]		3.590(2)		
C(31–71)···C(1–16)[5]		3.853(1)		

[1] $1+x,y,z$. [2] $-x,-y,1-z$. [3] $x,-1+y,-1+z$. [4] $1+x,-1+y,-1+z$. [5] $1-x,-y,1-z$. [6] $1-x,-y,-z$. [7] $-1+x,y,z$.

15e, and **16d**. Note that PIS on the amino group **a** are negative only for compounds **3b**, **13b** and **15b**, *i.e.*, all **b** protonation.

Basicity of N-*Aminoazoles.*—The comparison of the pK_a values for pairs of *N*-amino and *N*-methyl derivatives shows that when the protonation takes place on the azole ring (compounds **4**, **12** and **13**) the amino group acts as a withdrawing substituent decreasing the basicity of the azole. In the case of benzimidazole **12** and 2*H*-indazole **13** the basicity decreases 0.6 pK_a units. In the case of 4*H*-triazole the decrease is more important, about 1.2 pK_a units.

9-Aminocarbazole **17** clearly protonates on the amino group although its pK_a = 1.50 (Table 2) is much lower than that of 1,1-diphenylhydrazine ($pK_a \approx 3.7$)[31] due to the aromaticity of the carbazole ring (including the planarity of the phenyl rings). The comparison of the pK_as of 1-aminoindole (1.43) and 1-methylindole (−2.56) is conclusive evidence for the protonation of the first one in the amino group whereas the second protonates on the β-carbon.[8]

The pK_a values of Table 2 determined in water can be compared with those of Pozharskii[6] determined in CH_3CN: $pK_a(CH_3CN) = 5.45 + 1.49\ pK_a(H_2O)$, $n = 3$ (**11**, **12**, **13**), $r = 0.95$. The agreement is acceptable considering that two compounds protonate in the ring (**12**, **13**) and the third one in the amino group (**11**).

Semiempirical Calculations.—Semiempirical calculations were carried out within the INDO approximation[32] with complete optimisation of the geometry.[33]

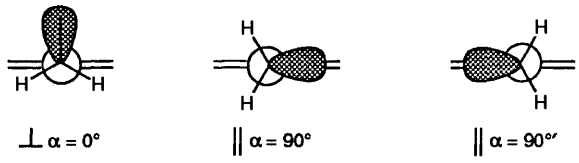


Fig. 3 Definition of the dihedral angle α

The 17 *N*-aminoazoles were already described.[1] Their corresponding INDO energies are given as 'Supplementary Material', together with those of all possible *N*-protonated salts (see Table 1). As in the preceding paper,[1] three conformations were calculated for the amino group: (i) α = 0° (perpendicular conformation ⊥) where the amino group lone pair is perpendicular to the ring plane; (ii) α = 90° and α = 90°″ (parallel conformations, ||) where the amino lone pair lies in the ring plane (for ring of C_s symmetry, α = 90° corresponds to the conformation in which the lone pair eclipses the Z part of the ring). In Fig. 3 are represented these situations (for more detail, see ref. 1).

A total of 77 INDO optimized geometries were calculated. The minimum energy conformations are slightly rotated about the 0°, 90° or 90°″ values, but the very flat potential energy curves preclude any firm conclusion about these deviations.

Geometries.—Ring geometries. The INDO calculated geometry for cation **12d** compares fairly well with those determined by crystallography for picrates **12dI** and **12dII**. The distances and angles between heavy atoms are correctly described, those

Table 6 ^{13}C NMR parameters (δ and J) of *N*-aminoazoles [PIS effects]

Compound	Solvent	C(2)	C(3)	C(4)	C(5)
2	[$^2H_6$]DMSO	136.9	—	126.1	121.2
		^1J 203.2		^1J 188.1	^1J 190.6
		^3J 6.2		^2J 10.5	^2J 15.8
		^3J 9.3		^3J 10.5	^3J 3.2
	CF_3CO_2H	133.7 [−3.2]	—	117.7 [−8.4]	122.7 [+1.5]
		^1J 225.1 [+21.9]		^1J 205.7 [+17.6]	^1J 206.4 [+15.8]
				^2J 11.1	^2J 11.4
				^3J 6.2	^3J 3.3
	H_2SO_4	132.2 [−4.7]	—	119.7 [−6.4]	119.1 [−2.1]
		^1J 231.5 [+28.3]		^1J 211.9 [+23.8]	^1J 213.1 [+22.5]
		^3J ^3J 5.5		^2J ^3J 8.0	^2J 12.5
		^2J 5.5		^2J 2.4	^3J ^3J 4.6
3	[$^2H_6$]DMSO	—	136.9	104.2	129.2
			^1J 186.7	^1J 177.0	^1J 189.2
			^2J 4.9	^2J 8.5	^2J 8.5
			^3J 9.7	^2J 9.8	^3J 3.6
	CF_3CO_2H	—	131.2 [−5.7]	106.3 [+2.1]	135.2 [+6.0]
			^1J 200.5 [+13.8]	^1J 190.3 [+13.3]	^1J 201.5 [+12.3]
			^2J 6.5	^2J 6.6	^2J 7.5
			^3J 6.5	^2J 6.6	^3J 5.4
	H_2SO_4	—	135.2 [−1.7]	108.5 [+4.3]	135.0 [+5.8]
			^1J 205.2 [+18.5]	^1J 194.6 [+17.6]	^1J 205.8 [+16.6]
			^2J 6.7	^2J 6.0	^2J 7.8
			^3J 6.7	^2J 6.0	^3J 5.5
Iodide **25**[24]	[$^2H_6$]DMSO	—	134.9	105.2	136.5
			^1J 199.4	^1J 189.3	^1J 201.8
				^2J 6.5	^2J 6.8
				^2J 6.5	^3J 5.3
4	[$^2H_6$]DMSO	—	144.8	—	144.8
			^1J 212.5	—	^1J 212.5
			^3J 4.3	—	^3J 4.3
	CF_3CO_2H	—	142.9 [−1.9]	—	142.9 [−1.9]
			^1J 227.7 [+15.2]	—	^1J 227.7 [+15.2]
			^3J 4.3	—	^3J 4.3
	H_2SO_4	—	140.8 [−4.0]	—	140.8 [−4.0]
			^1J 234.9 [+22.4]	—	^1J 234.9 [+22.4]
			^3J 3.9	—	^3J 3.9
5	[$^2H_6$]DMSO	—	149.0	—	142.4
			^1J 206.9	—	^1J 214.2
			^3J 12.6	—	^3J 6.4
					^3J 3.2
	CF_3CO_2H	—	140.3 [−8.7]	—	138.3 [−4.1]
			^1J 226.0 [+19.1]	—	^1J 228.8 [+14.6]
			^3J 7.8	—	^3J 2.9
	H_2SO_4	—	141.2 [−7.8]	—	138.8 [−3.6]
			^1J 233.7 [+26.8]	—	^1J 235.4 [+21.2]
			^3J 7.7	—	^3J 3.3

involving hydrogen atoms are not so good. The protonation of an azole produces an increase in the value of the endocyclic nitrogen angle of about 4.5° a result well documented both theoretically[34] and experimentally.[35]

Amino group geometries. The *N*-amino bond, N(1)–N(8), is the distance which shows the largest deviation when INDO calculated geometry and X-ray geometries for salt **12d** are compared, −0.07 for **I** and −0.06 Å for **II**. In all cases the protonation on a nitrogen atom of the azole ring produces a shortening of the N–NH_2 distance of about 0.01 Å while the protonation on the amino group does not effect this bond length.

Conformation of the amino group. In Table 10 are gathered the computed geometries of the amino group before[1] and after protonation on the nitrogen atoms of the azole ring. As in the case of neutral *N*-aminoazoles,[1] the sp^3 hybridisation is always favoured.

The most interesting result of Table 10 is that the protonation of the azole stabilises the perpendicular conformation ($\alpha = 0°$). For instance, for parallel conformations with $\alpha = 90°$, compounds **2**, **4**, **8** and **12**, the protonation induces a conformational change and the perpendicular conformation becomes the most stable. Protonation of the azole increases the electron demand of the ring favouring the perpendicular conformation where the amino lone pair can best interact with the azolium ring.

Relationships between Total Charge Densities and ^{15}N *Chemical Shifts.*—In the preceding paper,[1] we found linear relationships between ^{15}N chemical shifts and INDO calculated total charges for neutral compounds. Since the values in CF_3CO_2H and in H_2SO_4 of Table 8 are linearly related [eqns. (1)–(3)], we will report here only the equations for the last solvent.

$$\delta_{^{15}N}(NH_2) = -4573.9 + 826.7\,q(\pi + \sigma); \quad n = 8, R = 0.98 \quad (4)$$

$$\delta_{^{15}N}(N\text{-}NH_2) = 1858.2 - 426.5\,q(\pi + \sigma); \quad n = 8, R = 0.95 \quad (5)$$

Table 7 ^{13}C NMR parameters (δ and J) of *N*-aminobenzazoles [PIS effects]

Compound	Solvent	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(3a)	C(7a)
11	[$^2H_6$]DMSO	125.2 ^1J 186.9 ^2J 9.0	99.7 ^1J 174.1 ^2J 7.1 ^3J 3.0	119.4 ^1J 159.0 ^3J 7.0	120.5 ^1J 158.3 ^3J 7.3	121.6 ^1J 159.4 ^3J 7.9 ^2J 1.2	109.6 ^1J 162.2 ^3J 7.4	125.9	133.6
12	[$^2H_6$]DMSO	144.7 ^1J 207.9	—	119.6 ^1J 159.0 ^3J 8.6	121.7 ^1J 158.0 ^3J 7.9	122.5 ^1J 161.1 ^3J 8.0	110.2 ^1J 164.5 ^3J 8.2	141.5	135.0
	CF_3CO_2H	138.8 [−5.9] ^1J 220.9 [13.0]	—	113.3 [−6.3] ^1J 170.5 [11.5] ^3J 7.6	126.0* [4.3] ^1J 165.8 [7.8] ^3J 7.6	126.4* [3.9] ^1J 165.4 [4.3] ^3J 7.5	110.3 [0.1] ^1J 170.4 [5.9] ^3J 7.9	130.6 [−10.9]	128.1 [−6.9]
	H_2SO_4	136.0 [−8.7] ^1J 228.1 [20.2] ^2J 6.5 (NH)	—	114.6 [−5.0] ^1J 173.7 [14.7] ^3J 6.8	128.7 [7.0] ^1J 168.2 [10.2] ^3J 6.5	128.7 [6.2] ^1J 168.2 [7.1] ^3J 6.5	110.1 [−0.1] ^1J 172.8 [8.3] ^3J 7.5	126.8 [−14.7]	125.8 [−9.2]
12 Picrate	[$^2H_6$]DMSO	141.5 ^1J 221.0	—	114.7 ^1J 167.8 ^3J 7.5	126.0 ^1J 164.9 ^3J 7.7	126.5 ^1J 164.5 ^3J 7.2	112.8 ^1J 170.5 ^3J 7.3	132.0	129.6
		δ C(1′) 161.0; δ C(3′) 125.3, ^1J 168.1, ^3J 5.7; δ C(2′) 141.8; δ C(4′) 124.5							
13	[$^2H_6$]DMSO	—	119.9 ^1J 194.6 ^4J 1.8	119.9 ^1J 161.3 ^3J 7.4	120.6 ^1J 159.0 ^3J 7.8	124.7 ^1J 160.7 ^3J 8.3	116.3 ^1J 163.1 ^3J 7.0	120.6	145.2
	CF_3CO_2H	—	129.9 [10.0] ^1J 201.7 [7.1] ^4J 1.7	120.6 [0.7] ^1J 173.8 [12.5]	124.2 [3.6] ^1J 165.5 [6.5] ^3J 7.2 ^2J 1.7	132.5 [7.8] ^1J 164.9 [4.2] ^3J 8.2	109.5 [−6.8] ^1J 170.8 [7.7] ^3J 8.1	117.9 [−2.7]	137.0 [−8.2]
	H_2SO_4	—	131.4 [11.5] ^1J 207.7 [13.1]	121.8 [1.9] ^1J 174.8 [13.5] ^3J 7.3	126.7 [6.1] ^1J 167.5 [8.5] ^3J 7.2	136.6 [11.9] ^1J 167.4 [6.7] ^3J 8.1	110.1 [−6.2] ^1J 174.5 [11.4] ^3J 7.3	117.8 [−2.8]	138.7 [−6.5]
13 Picrate	[$^2H_6$]DMSO	—	121.4 ^1J 195.8	120.36 ^1J 162.3 ^3J 7.8	121.3 ^1J 160.0 ^3J 7.6	125.9 ^1J 160.1 ^3J 8.6	115.5 ^1J 163.7 ^3J 7.2 ^4J 1.2	120.42	144.0
		δ C(1′) 160.5; δ C(3′) 125.3, ^1J 168.4, ^3J 5.7; δ C(2′) 141.9; δ C(4′) 125.0							

15	$[^2H_6]$DMSO	—	—	116.4 ^1J 161.8	125.0 ^1J 159.0 ^3J 8.2	125.0 ^1J 159.0 ^3J 8.2	116.4 ^1J 161.8	141.9 ^3J 9.0 ^3J 5.4	141.9 ^3J 9.0 ^3J 5.4
	CF_3CO_2H	—	—	114.9 [−1.5] ^1J 170.2 [8.4] ^3J 4.8	126.0 [1.0] ^1J 163.2 [4.2] ^3J 8.1	126.0 [1.0] ^1J 163.2 [4.2] ^3J 8.1	114.9 [−1.5] ^1J 170.2 [8.4] ^3J 4.8	140.3 [−1.6] ^3J 9.4 ^3J 5.5	140.3 [−1.6] ^3J 9.4 ^3J 5.5
	H_2SO_4	—	—	114.6 [−1.8] ^1J 176.8 [15.0] ^3J 4.7	132.1 [7.1] ^1J 166.7 [7.7] ^3J 7.5	132.1 [7.1] ^1J 166.7 [7.7] ^3J 7.5	114.6 [−1.8] ^1J 176.8 [15] ^3J 4.7 [15.0]	135.3 [−6.6] ^3J 9.7 ^3J 5.3	135.3 [−6.6] ^3J 9.7 ^3J 5.3
16	$[^2H_6]$DMSO	—	—	119.1 ^1J 164.6 ^3J 7.7	123.8 ^1J 161.4 ^3J 7.8	127.1 ^1J 161.8 ^3J 8.0 ^2J 1.5	110.4 ^1J 169.1 ^3J 8.1	144.0	132.4
	CF_3CO_2H	—	—	112.7 [−6.4] ^1J 175.5 [10.9] ^3J 5.6	130.0 [6.2] ^1J 167.7 [6.3] ^3J 7.9	130.4 [3.3] ^1J 167.5 [5.7] ^3J 7.8	111.1 [0.7] ^1J 175.6 [6.5] ^3J 5.5	133.8 [−10.2]	131.6 [−0.8]
	H_2SO_4	—	—	113.8 [−5.3] ^1J 178.7 [14.1]	133.0 [9.2] ^1J = 170.3 [8.9] ^3J 6.3	133.7 [6.6] ^1J 170.3 [8.5] ^3J 7.2	110.3 [−0.1] ^1J 179.2 [10.1] ^3J 6.9	133.3 [−10.7] ^3J 10.6 ^3J 4.7	129.8[−2.6]

		C(1)/C(8)	C(2)/C(7)	C(3)/C(6)	C(4)/C(5)	C(4a)/C(4b)	C(8a)/C(9a)
17	$[^2H_6]$DMSO	109.0 ^1J 162.8 ^3J 7.9	125.4 ^1J 160.0 ^3J 7.7	118.5 ^1J 159.9 ^3J 7.4	119.9 ^1J 158.9 ^3J 8.1	119.7	141.1

Table 8 ^{15}N NMR parameters (δ and J) of *N*-amino-azoles and -benzazoles [PIS effects]

Compound	Solvent	NH_2	N(1)	N(2)	N(3)	N(4)
2	[$^2H_6$]DMSO	−311.4 ^1J(n.o.)	−198.7	—	−126.8	—
	CF_3CO_2H	−309.0 [+2.4]	−193.4 [+5.3]	—	−217.0 [−90.2] ^1J 102.8 ^2J ^2J 4.5 ^3J 3.9	—
	H_2SO_4	−308.4 [+3.0]	−214.1 [−15.4] ^2J 12.9 ^3J 2.0	—	−209.8 [−83.0] ^1J 104.5 ^2J ^2J 4.0 ^3J 3.8	—
3	[$^2H_6$]DMSO	−295.1 ^1J 71.0	−162.1	−72.4	—	—
	CF_3CO_2H	−305.1 [−10.0]	−177.4 [−15.3] ^2J 10.1 ^3J 3.5	−178.4 [−106.0] ^2J 10.5 ^3J 5.6	—	—
	H_2SO_4	−301.8 [−6.7]	−186.0 [−23.9] ^2J 10.4 ^3J 3.3	−195.2 [−122.8] ^1J 110.8 ^2J 10.6 ^3J ^3J 5.6	—	—
4	[$^2H_6$]DMSO	−315.5 ^1J 70.0	−66.1	−66.1	—	−198.2
	CF_3CO_2H	−313.2 [+2.3]	−133.4 [−67.3]	−133.4 [−67.3]	—	−190.4 [+7.8]
	H_2SO_4	−308.8 [+6.7]	−131.9 [−65.8] ^2J 12.0	−131.9 [−65.8] ^2J 12.0	—	−209.6 [−11.4] ^2J 10.7
5	[$^2H_6$]DMSO	−303.0 ^1J 72.1	−155.7	−79.8	—	−131.6
	CF_3CO_2H	−301.1 [+1.9]	−152.1 [+3.6] ^2J 12.1	−78.8 [+1.0] ^2J 13.3	—	−211.2 [−79.6] ^2J 6.5
	H_2SO_4	−299.8 [+3.2]	−174.5 [−18.8] ^2J 13.0	−90.1 [−10.3] ^2J 14.1	—	−205.3 [−73.7]
11	[$^2H_6$]DMSO	−315.1 ^1J 71.2	−202.2 ^2J 8.5	—	—	—
12	[$^2H_6$]DMSO	−317.8 ^1J 71.9	−215.8 ^2J 9.5	—	−143.6 ^2J 11.9	—
	CF_3CO_2H	−317.3 [+0.5]	−209.2 [+6.6]	—	−234.0 [−90.4] ^1J 104.3	—
	H_2SO_4	−312.0 [+5.8]	−229.1 [−13.3] ^2J 8.2	—	−224.7 [−81.1] ^1J 104.6 ^2J 3.6	—
13	[$^2H_6$]DMSO	−289.1 ^1J 70.5	−94.8	−145.5	—	—
	CF_3CO_2H	−301.3 [−12.2]	−204.6 [−109.8]	−172.9 [−27.4]	—	—
	H_2SO_4	−300.1 [−11.0]	−212.6 [−117.8]	−196.4 [−50.9]	—	—
14	[$^2H_6$]DMSO	−305.9	−184.6	−56.3	—	—
15	[$^2H_6$]DMSO	−275.3 ^1J 73.1	−83.6	−99.9	−83.6	—
	CF_3CO_2H	−284.8 [−9.5]	−120.7 [−37.1]	−95.5 [+4.4]	−120.7 [−37.1]	—
	H_2SO_4	−285.8 [−10.5]	−132.7 [−49.1]	−112.1 [−12.2]	−132.7 [−49.1]	—
16	[$^2H_6$]DMSO	−307.7 ^1J 73.4	−148.2	−2.3	−50.8	—
	CF_3CO_2H	−303.1 [+4.6]	−143.1 [+5.1]	−32.0 [−29.7]	−168.3 [−117.5]	—
	H_2SO_4	−300.5 [+7.2]	−163.9 [−15.7]	−39.1 [−36.8]	−160.6 [−109.8]	—

$$\delta_{^{15}N}(N\text{-protonated}) = 2337.7 - 505.9\,q(\pi + \sigma); \quad n = 6,\ R = 0.87 \quad (6)$$

The slopes and correlation coefficients are similar to those previously described.[1] Eqns. (4)–(6) were calculated using the total charges corresponding to the most stable cation (for compounds, such as **4** and **15**, where there are two equivalent protonation sites, the mean value of both total charges has been used). The use of the charges of less stable cations, for instance **5d** and **16b**, yields poorer relationships ($R < 0.8$).

Proton Affinities of N-*Aminoazoles.*—Table 11 contains all the values of ΔEp (calculated as the INDO//INDO energy difference between the neutral and the protonated form) and of PAs. The empirical equations relating both magnitudes were devised in two preceding publications.[36,37]

Andrianov, Shoken and Eremeev,[38] have calculated (STO-3G//MNDO) the proton affinities of *N*-aminoazoles (from pyrrole to pentazole) assuming a protonation on the amino group. Their values are considerably different from ours (for instance, 1-aminopyrrole, PA = 249.0 kcal mol^{-1}, to compare

Table 9 ^{13}C and ^{15}N protonation induced shifts, $\Delta\delta$ (ppm)

	N-Methyl[8]					*N*-Amino					
Comp.	**b**	**c**	**d**	**e**	*N*-CH_3	**b**	**c**	**d**	**e**	*N*-NH_2	**a**(NH_2)
2	CH: —	N: −94.9[b]	CH: —	CH: —	+9.2[b]	CH: −3.2[b]	N: −90.2[b]	CH: −8.4[b]	CH: +1.5[b]	+5.3[b]	+2.4[b]
	CH: −4.0[c]	N: —	CH: −10.6[c]	CH: +2.4[c]	—	CH: −4.7[d]	N: −83.0[d]	CH: −6.4[d]	CH: −2.1[d]	−15.4[d]	+3.0[d]
3	N: −111.6[b]	CH: −4.8[b]	CH: +2.6[b]	CH: +5.7[b]	−10.0[b]	N: −106.0[b]	CH: −5.7[b]	CH: +2.1[b]	CH: +6.0[b]	−15.3[b]	−10.0[b]
	N: —	CH: −4.8[d]	CH: +2.7[d]	CH: +5.8[d]	—	N: −122.8[d]	CH: −1.7[d]	CH: +4.3[d]	CH: +5.8[d]	−23.9[d]	−6.7[d]
4	CH: −0.8[a]	N: −70.7[b]	N: −70.7[b]	CH: −0.8[a]	+11.0[b]	CH: −1.9[b]	N: −67.3[b]	N: −67.3[b]	CH: −1.9[b]	+7.8[b]	+2.3[b]
	CH: −0.5[c]	N: —	N: —	CH: −0.5[c]	—	CH: −4.0[d]	N: −65.8[d]	N: −65.8[d]	CH: −4.0[d]	+11.4[d]	+6.7[d]
5	N: +0.7[b]	CH: −9.0[a]	N: −83.8[b]	CH: −3.0[a]	+7.0[b]	N: +1.0[b]	CH: −8.7[b]	N: −79.6[b]	CH: −4.1[b]	+3.6[b]	+1.9[b]
	N: —	CH: —	N: —	CH: —	—	N: −10.3[d]	CH: −7.8[d]	N: −73.7[d]	CH: −3.6[d]	−18.8[d]	+3.2[d]
12	C(7a): −2.2[a]	C(3a): −10.0[a]	N: −94.1[b]	CH: −1.0[a]	+10.6[b]	C(7a): −6.9[b]	C(3a): −10.9[b]	N: −90.4[d]	CH: −5.9[b]	+6.6[b]	+0.5[b]
	C(7a): −5.7[c]	C(3a): −13.1[c]	N: —	CH: −5.4[c]	—	C(7a): −9.2[d]	C(3a): −14.7[d]	N: −81.1[d]	CH: −8.7[d]	−13.3[d]	+5.8[d]
13	N: −118.1[b]	C(7a): —	C(3a): —	CH: —	−23.6[b]	N: −109.8[b]	C(7a): −8.2[b]	C(3a): −2.7[b]	CH: +10.0[b]	−27.4[b]	−12.2[b]
	N: —	C(7a): −9.9[c]	C(3a): −2.7[c]	CH: +9.1[c]	—	N: −117.8[d]	C(7a): −6.5[d]	C(3a): −2.8[d]	CH: +11.5[d]	−50.9[d]	−11.0[d]
14	N: −123.2[b]	CH: —	C(3a): —	C(7a): —	−14.5[b]	N:[e]	CH:[e]	C(3a):[e]	C(7a):[e]	*e*	*e*
	N: —	CH: −4.3[c]	C(3a): −4.9[c]	C(7a): −1.0[c]	—	N:[e]	CH:[e]	C(3a):[e]	C(7a):[e]	*e*	*e*
15	N: −28.6[b]	C(3a): —	C(7a): —	N: −28.6[b]	−14.4[b]	N: −37.1[b]	C(3a): −1.6[b]	C(7a): −1.6[b]	N: −37.1[b]	+4.4[b]	−9.5[b]
	N: —	C(3a): −7.4[c]	C(7a): −7.4[c]	N: −52.4[d]	−24.2[d]	N: −49.1[d]	C(3a): −6.6[d]	C(7a): −6.6[d]	N: −49.1[d]	−12.2[d]	−10.5[d]
16	N: −26.6[b]	N: −120.6[b]	C(3a): −11.8[a]	C(7a): +0.6[a]	+6.0[b]	N: −29.7[b]	N: −117.5[b]	C(3a): −10.2[b]	C(7a): −0.9[b]	+5.1[b]	+4.6[b]
	N: —	N: —	C(3a): −12.5[c]	C(7a): +0.1[c]	—	N: −36.8[d]	N: −109.8[d]	C(3a): −10.7[d]	C(7a): −2.6[d]	−15.7[d]	+7.2[d]

[a] CF_3CO_2H–$CDCl_3$. [b] CF_3CO_2H–[$^2H_6$]DMSO. [c] SO_4H_2–$CDCl_3$. [d] SO_4H_2–[$^2H_6$]DMSO. [e] Rearrange in acid medium (see text).

Table 10 Effect of the protonation in the azole ring on the conformation of the *N*-amino group (α values; sp^3 hybridization)

	α (Neutral azole)[1]				α (Azolium cation)		
	0°	90°	90°′		0°	90°	90°′
Imidazole **2**	1.3	0	0.4	**2c**	0	0.6	1.5
Pyrazole **3**	1.6	1.2	0	**3b**	1.3	0.3	0
4*H*-1,2,4-Triazole **4**	0.5	0	—	**4c**	0	0.9[a]	1.3
1*H*-1,2,4-Triazole **5**	1.6	1.4	0	**5b**	1.1	0.4	0
				5d	0	2.6	0.3
2*H*-1,2,3-Triazole **6**	0.1	0	—	**6b**	0	0.3[a]	1.5
1*H*-1,2,3-Triazole **7**	1.3	0.7	0	**7b**	0.3	0	0.2
				7c	0	2.2	1.5
2*H*-Tetrazole **8**	0.4	0	0.3	**8b**	0	0.6	2.2
				8c	0	2.7	3.4
				8e	0	1.0	0
1*H*-Tetrazole **9**[b]	0.9	1.0	0	**9b**	0	0.1	0
				9c	0	2.4	1.3
				9d	0	2.2	0.4
1*H*-Benzimidazole **12**[b]	2.3	0	0.7	**12d**	0	0	1.1
2*H*-Indazole **13**	0	1.7	0.4	**13b**	0	0.7	0
1*H*-Indazole **14**	2.6	0.7	0	**14e**	2.7	0.1	0
2*H*-Benzotriazole **15**	0	2.6	—	**15b**	0	2.1[a]	3.1
1*H*-Benzotriazole **16**	2.2	0.3	0	**16d**	0	1.3	1.0
				16e	2.3	0	0.3

[a] The amino nitrogen lone pair eclipses the N^+–H proton. [b] There is an error in ref. 1 concerning most stable conformation.

Table 11 Protonation energies and proton affinities from INDO//INDO calculations (values in kcal mol^{-1})

Compound Amino	ΔE_p		PA	
	NH_2	–N=	NH_2[a]	–N=[b]
1-Pyrrole **1**	324.9	—	204.6	—
1-Imidazole **2**	320.1	371.4	201.7	224.0
1-Pyrazole **3**	322.2	359.8	202.9	214.2
4-1,2,4-Triazole **4**	314.3	366.4	198.1	219.8
1-1,2,4-Triazole **5**	317.2	361.6[c]	199.9	215.7
2-1,2,3-Triazole **6**	316.6	350.9	199.5	206.7
1-1,2,3-Triazole **7**	318.5	362.9[d]	200.7	216.8
2-Tetrazole **8**	312.8	355.2[e]	197.2	210.3
1-Tetrazole **9**	311.7	356.5[f]	196.6	211.4
1-Indole **11**	331.5	—	208.5	—
1-Benzimidazole **12**	326.2	377.0	205.3	228.8
2-Indazole **13**	320.4	375.1	201.8	227.2
1-Indazole **14**	330.9	361.6	208.2	215.7
2-Benzotriazole **15**	313.3	364.3	197.5	218.0
1-Benzotriazole **16**	326.6	369.9[g]	205.6	222.8
9-Carbazole **17**	337.7	—	212.3	—

[a] From $PA(NH_2) = 8.0 + 0.605\ [\Delta E_p(NH_2)]$. [b] From $PA(–N=) = -90.9 + 0.848\ [\Delta E_p(–N=)]$. [c] Protonation on N^4 (**5d**). [d] Protonation on N^3 (**7c**). [e] Protonation on N^4 (**8c**). [f] Protonation on N^4 (**9d**). [g] Protonation on N^3 (**16c**).

Table 12 Relative stabilities of azolium cations in kcal mol^{-1} (from calculated PAs)

Amino derivative	N^1	N^2	N^3	N^4
1-1,2,4-Triazole	—	7.1 (**5b**)	—	0 (**5d**)
1-1,2,3-Triazole	—	16.3 (**7b**)	0 (**7c**)	—
2-Tetrazole	11.6 (**8e**)	—	16.8 (**8b**)	0 (**8c**)
1-Tetrazole	—	14.7 (**9b**)	4.3 (**9c**)	0 (**9d**)
1-Benzotriazole	—	20.0 (**16e**)	0 (**16d**)	—

with our estimation of 204.6 kcal mol^{-1})* and are only very roughly correlated: $PA_{STO\text{-}3G} = -347 + 2.9\ PA_{INDO}$, $n = 9$, $R = 0.83$ (10).

Another interesting comparison concerns the PA values for a particular azole of all the cations obtained by protonation on the azole ring. This allows comparison of the relative stabilities of azolium cations when there are several possibilities (Table 12).

Always the preferred cation is that protonated at the most remote nitrogen atom (positions **c** and **d**): **5d**, **7c**, **8c**, **9d** and **16d**. When two of such positions are available, **9c** and **9d**, the difference in stability is small. Experimental evidence exists also for other substituents on the nitrogen than an amino group (H, methyl, phenyl);[39] in all cases, there is an agreement with the INDO//INDO calculations: 1*H*-1,2,4-triazole,[39a] 1*H*-1,2,3-triazole,[39b] 1*H*-tetrazole[39c] and 1*H*-benzotriazole.[39a,40] In the case of 2*H*-tetrazole there is no experimental evidence to sustain the structure **8c**.

To calculate the annellation effect on the difference in PA between the protonation on the azole and the protonation on the amino group we have calculated the differences **2a–2c** (imidazole)/**12a–12d** (benzimidazole), **3a–3b** (pyrazole)/**14a–14e** (1*H*-indazole), **7a–7c** (1*H*-1,2,3-triazole protonated on N^3)/**16a–16d** (1*H*-benzotriazole protonated on N^3) and **7a–7b** (1*H*-1,2,3-triazole protonated on N^2)/**16a–16e** (1*H*-benzotriazole protonated on N^2). These values are linearly related,

$$\delta PA_{BzAz} = -3.52 + 1.2\,\delta PA_{Az},\ n = 4,\ R = 0.99 \quad (11)$$

showing that the annellation effect is small. The effect of the annellation is very different in the *ortho*-quinonoid structures of 2*H*-indazole and 2*H*-benzotriazole: **3a–3b** (pyrazole)/**13a–13b** (2*H*-indazole) and **6a–6b** (2*H*-1,2,3-triazole)/**15a–15b** (2*H*-benzotriazole): $\delta PA_{isoBzAz} = 11.9 + 1.2\ \delta PA_{Az}$ (12). In this case, the iso-annellation increases the difference in basicity between the basic sites due to an increase in the basicity of the ring whereas the amino basicity is rather insensitive.

Before ending, we must make a last comment about the protonation of *N*-aminoindole **11**. To estimate the pK_a corresponding to its β-protonation we have carried out a STO-3G calculation on the INDO optimized geometry (STO-3G//INDO). This calculation gives a value of −10.999 hartrees† for the binding energy of the 1s orbital of the carbon C(3). An equation we reported previously,[41] relates this energy to the proton affinity (PA), thus a value of 209.4 kcal mol^{-1} could be calculated for the PA of C(3). In another paper,[42] we described the linear relationship between pK_a and PA for indoles; using the corresponding equation, the pK_a for the β-protonation on *N*-aminoindole could be estimated to be −2.7. The experimental value ($pK_a = 1.43$, Table 2) clearly corresponds to the protonation of the amino group (note that the pK_a for the *C*-protonation of indole is −2.56, Table 2, very close to that calculated for **11**).

In summary, the work here described on the protonation site and basicity of *N*-aminoazoles completes the knowledge of this family of compounds which has been recently reviewed.[43]

Supplementary Material.—Lists of atomic coordinates and thermal components for non-hydrogen atoms, hydrogen parameters and bond distances and angles have been deposited at the Cambridge Crystallographic Data Centre.‡ Two Tables with the INDO//INDO energies (in kcal mol^{-1}) for neutral and protonated *N*-aminoazoles have been deposited.§

* 1 cal = 4.18 J.

† 1 hartree ≈ 4.36×10^{-18} J.

‡ For details of the CCDC deposition scheme, see 'Instructions for Authors,' *J. Chem. Soc., Perkin Trans. 2*, 1993, issue 1.

§ Supp. Pub. No. 56955 (2 pp.). For details of the supplementary publications scheme, see 'Instructions for Authors,' *J. Chem. Soc., Perkin Trans. 2*, 1993, issue 1.

Acknowledgements

Thanks are given to the CICYT (Spain) for financial support (projects PB90-0070 and PB-90-226-C02). One of us (N. A. G.) is indebted to MEC of Spain for a grant during his sabbatical stay at the Universidad Autónoma de Madrid.

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Paper 3/01294H
Received 5*th March* 1993
Accepted 10*th May* 1993